REMARKS

Amendments to the Specification

The specification has been amended to address the Office's comments regarding the use of various trademarks in the application, including "TAQMAN" and "RNEASY". Specifically, the specification has been amended to capitalize all of the trademark names where found in the specification.

No new matter has been added by way of these amendments.

Amendments to the Claims

Claims 1, 3-4, 6, 16, and 26-28 are pending in this application. Claims 5, 7-15, and 18-25 have been withdrawn without prejudice, as directed to non-elected subject matter. Claim 2 and claim 17 were previously canceled without prejudice. Claims 1, 3, and 16 have been amended.

Claim 1 has been amended to recite that the PAK polypeptide is a PAK1 polypeptide comprising SEQ ID NO: 7 and the PAK nucleic acid is a nucleic acid encoding said polypeptide. Amended claim 1 finds support in the as-filed application at, *inter alia*, pages 2, 4 and 5.

Claim 3 has been amended to recite that the cultured cells have a defect in G1 DNA damage checkpoint or the G2 DNA damage checkpoint function. Amended claim 3 finds support in the as-filed application at, *inter alia*, pages 9-10, 23, and 25.

Claim 4 has been amended to recite that the PAK polypeptide in the assay system is a PAK1 polypeptide comprising SEQ ID NO: 7. Amended claim 4 finds support in the as-filed application at, *inter alia*, pages 4 and 5.

Claim 16 has been amended to recite that the second assay system is capable of detecting a change in the G1 DNA damage checkpoint pathway or the G2 DNA damage checkpoint pathway. Amended claim 16 finds support in the as-filed application at, *inter alia*, pages 1-4.

Claim 26 recites that the agent specifically binds to the PAK1 polypeptide or nucleic acid (of claim 1). Amended claim 26 finds support in the as-filed application at, *inter alia*, pages 3 and 13-20.

The claim amendments are made solely in an effort to advance prosecution and are made without prejudice or disclaimer, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. Additionally, these amendments and cancellation are not and should not be construed as admissions regarding the patentability of the claimed or canceled subject matter. Applicants reserve the right to pursue the subject matter of previously presented claims in this or in any other appropriate patent application. No new matter has been added by way of these amendments. Accordingly, Applicants respectfully request the entry of the amendments presented.

Objection to the Specification

The specification was objected to because the trademarks in the application were not capitalized. The specification has been amended to address this objection. Applicant respectfully requests withdrawal of the objection to the specification.

35 USC § 112, First Paragraph, Rejections

Enablement

Claims 1, 3-4, 6, and 16 remain rejected and new claims 26-28 are rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse the rejections.

The Office Action argued that the claims are not enabled because allegedly they contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the Office appears confused as to what the term "PAK" encompasses ("PAK is considered to here to

be a member of the genus of PAKs and other PAKs would have a name other than PAK".) Office Action, at page 3. The claims have been amended to recite that the PAK is PAK1 comprising SEQ ID NO: 7. Thus, the Applicants submit that the term "PAK" is clear.

Further, the Office alleged that the claims are not enabled because they broadly encompass assaying cells expressing any PAK and therefore the skilled artisan would not know what agents modulate the expression and/or activity of PAK. Claims 1 and 4 have been amended to specify that the PAK is PAK1 (SEQ ID NO: 7). The Office further alleged that the phrase "defective CHK function" is not defined in the specification and could be any type of altered cell cycle regulation, including regulation that may not involve p21 activated kinases. Claims 3 and 16 have been amended to specify that the CHK function or pathway refers to the G2 DNA damage checkpoint or the G1 DNA damage checkpoint function or pathway. Applicants submit that the claims, as amended, are fully enabled.

Under 35 U.S.C. §112, all that is required for satisfaction of the enablement requirement is that the specification describe the invention in such terms as to enable one skilled in the art to make and use the invention. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. In re Wands, 858 F.2d 731 (Fed. Cir. 1988); United States v. Telectronics, Inc., 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01.

The instant specification provides considerable guidance to enable a skilled artisan to make and use the claimed screening assays. Initially, the specification teaches that PAK polypeptides and the CHK pathway are involved in the biological processes relating to cell cycle regulation and cell growth (specification, pages 1-4). The specification also directly teaches that PAK polypeptides are p21 activated kinases involved in the regulation of cytoskeletal dynamics, i.e, cell proliferation (specification, page 2). In addition, the specification clearly explains the relationship between chk1, PAK, and the CHK pathway. Specifically, the specification teaches on pages 3, 4 and

34-36 that Chk1 is a gene that modifies the CHK pathway in Drosophila and that PAK is the human ortholog of Chk1.

In addition, the specification describes in detail the characteristics of PAK1 polynucleotides and polypeptides and further provides the amino acid sequence of PAK1 (SEQ ID NO: 7) and the nucleotide sequences of the corresponding polynucleotides that can be used in the cell culture assay systems. See specification at pages 4-7. In addition, the specification teaches one how to produce cells that express PAK1 polypeptides or nucleic acids at pages 8-10 and how to use them in cell proliferation and cell cycle assays at pages 24-25.

In addition, the specification describes agents that modulate the expression and/or activity of a PAK1 nucleic acid or polypeptide, including PAK1-specific antibodies, PAK1-specific antisense oligomers and other nucleic acid modulators (ie RNAi), and chemical agents or small molecules that specifically bind to or interact with PAK1, or compete with a PAK1 binding partner (specification, pages 12-19) and provides several specific examples of such agents (specification at pages 13-14 (small molecule modulating agents), pages 14-17 (protein modulating agents), and pages 18-19 (nucleic acid modulating agents).

Furthermore, the specification teaches that the assay system can be a cell-based assay and provides examples of cell-based assay systems, including cell proliferation assay systems (specification at pages 24-25). In addition, the specification teaches one skilled in the art how to measure the expression and/or activity of PAK1. For example, the specification teaches that a change in the expression of PAK1 can be determined using western blotting, immunoprecipitation, and immunohistochemical analyses to determine protein levels, as well as Taqman, RT-PCR, Northern blotting, and other analyses to determine mRNA levels (pages 36-39). The specification teaches that a change in the activity of PAK1 can be determined using kinase assays, such as the kinase assay described on pages 36-37, as well as other kinase assays well-known in the art.

In addition, with respect to claim 16, the specification provides numerous examples of assay systems that can be used to confirm that the test agent modulates the CHK pathway. (specification at pages 30-32).

In addition, the specification provides experimental data which demonstrated that PAK1 polynucleotide (encoding PAK1 polypeptide comprising SEQ ID NO: 7) is overexpressed in tissue samples of liver cancer, lung cancer, and pancreas cancer, as compared with matched normal tissues. Cells with overexpressed PAK were also shown to form colonies in soft agar, indicating abnormal proliferative properties. In addition, studies showed that overexpression of PAK1 resulted in increased expression of various transcription factors, including EGR, ETS1, E2F, and CREB. Specification at pages 37-39.

Further studies showed that siRNA targeted to a PAK1 polynucleotide (which encodes the PAK1 polypeptide comprising SEQ ID NO: 7) caused a decrease in cell proliferation in a breast cancer cell line, MCF7, and in a small cell lung cancer cell line, LX1. siRNA targeted to PAK1 polynucleotide was also shown to increase G1 cell cycle arrest in LX1 cells, resulting in apoptosis-associated DNA degradation in these cells.

Applicants submit that, based on the discussions presented above, there is ample support for the specification being enabling. That is, using the guidance and teachings provided in the specification, one skilled in the art would be able to make and use the claimed screening assays, which are directed to identifying a candidate CHK pathway modulating agent using an assay system comprising cultured cells that express a PAK1 polypeptide or nucleic acid. Applicants have taught one skilled in the art how to perform each and every step of the claimed methods. Further, Applicants have fully described the structure of the PAK1 polypeptide and PAK1 nucleic acid used in the claimed assays and have experimentally shown the connection between PAK1 and cell cycle regulation (CHK pathway). Applicants have even further provided a working example of a candidate CHK pathway modulating agent. An siRNA directed against PAK1 was shown to modulate the CHK pathway by causing G1 cell cycle arrest (apoptosis) in LX1 small cell lung cancer cells. Thus, Applicants have shown that an assay system comprising cultured cells that express a PAK1 polypeptide comprising SEQ ID NO: 7 or a nucleic acid encoding said polypeptide can be used to identify candidate CHK pathway modulating agents.

For the reasons set forth above, the claims are fully enabled and can be readily practiced by one skilled in the art. Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 112, first paragraph, rejection.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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